

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: David R. Dilley, Dina K. Kadyrzhanova, Zhenyong Wang
and Toni M. Warner

Application No.: 0 / Group No.:

Filed: Examiner:

For: **MODIFIED SYNTHETASES TO PRODUCE PENICILLINS AND CEPHALOSPORINS
UNDER THE CONTROL OF BICARBONATE**

Box Sequence

Assistant Commissioner for Patents
Washington, D.C. 20231SUBMISSION OF "SEQUENCE LISTING," COMPUTER READABLE COPY,
AND/OR AMENDMENT PERTAINING THERETO
FOR BIOTECHNOLOGY INVENTION CONTAINING NUCLEOTIDE
AND/OR AMINO ACID SEQUENCE

(check and complete this item, if applicable)

- 1.
- ☐
- This replies to the Office Letter dated _____.

NOTE: If these papers are filed before the office letter issues, adequate identification of the original papers should be made, e.g., in addition to the name of the inventor and title of invention, the filing date based on the "Express Mail" procedure, the application number from the return post card or the attorney's docket number added.

- ☐
- A copy of the Office Letter is enclosed.

CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10*

(When using Express Mail, the Express Mail label number is mandatory;
Express Mail certification is optional.)

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

- ☒
- deposited with the United States Postal Service in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

37 C.F.R. § 1.8(a)

37 C.F.R. § 1.10*

- ☐
- with sufficient postage as first class mail.

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Mailing Label No. _____ (mandatory)

TRANSMISSION

EJ715841669US

- ☐
- transmitted by facsimile to the Patent and Trademark Office.

Signature

Date: 10/06/99Tammi L. Taylor
Tammi L. Taylor

(type or print name of person certifying)

*WARNING: Each paper or fee filed by Express Mail **must** have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. § 1.10(b)."Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will **not** be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.

(Submission—Nucleotide and/or Amino Acid Sequence [9-37]—page 1 of 6)

IDENTIFICATION OF PERSON MAKING STATEMENT

2. I, Ian C. McLeod

(type or print name of declarant signing below)

state the following:

ITEMS BEING SUBMITTED

3. Submitted herewith is/are:

(check each item as applicable)

- A. ☒ "Sequence Listing(s)" for the nucleotide and/or amino acid sequence(s) in this application. Each "Sequence Listing" is assigned a separate identifier as required in 37 C.F.R. § 1.821(c) and 37 C.F.R. §§ 1.822 and 1.823.
- B. ☐ An amendment to the description and/or claims, wherein reference is made to the sequence by use of the assigned identifier, as required in 37 C.F.R. § 1.821(d).
- C. ☒ A copy of each "Sequence Listing" submitted for this application in computer readable form, in accordance with the requirements of 37 C.F.R. §§ 1.821(e) and 1.824.
- D. ☐ Please transfer to this application, in accordance with 37 C.F.R. § 1.821(e), the computer readable copy(ies) from applicant's other application identified as follows:

In re application of:

Application No.: 0 /

Filed:

For:

Group No.:

Examiner:

The Computer readable form(s) of applicant's other application corresponds to the "Sequence Identifier(s)" of the application as follows:

Computer Readable Form
(other application)

"Sequence Identifier"
(this application)

NOTE: "If the computer readable form of a new application is to be identical with the computer readable form of another application of the applicant on file in the Office, reference may be made to the other application and computer readable form in lieu of filing a duplicate computer readable form in the new application. The new application shall be accompanied by a letter making such reference to the other application and computer readable form, both of which shall be completely identified." 37 C.F.R. § 1.821(e).

- E. ☒ A statement that the content of each "Sequence Listing" submitted and each computer readable copy are the same, as required in 37 C.F.R. § 1.821(g).
- ☐ Because the statement is not made by a person registered to practice before the Office, the statement is verified as required in 37 C.F.R. § 1.821(b).
- F. ☒ Because this submission is made in fulfilling the requirement under 37 C.F.R. § 1.821(g), a statement that the submission includes no new matter.
- ☐ Because the statement is not made by a person registered to practice before the Office, the statement is verified, as required in 37 C.F.R. § 1.821(g).

**STATEMENT THAT "SEQUENCE LISTING"
AND COMPUTER READABLE COPY ARE THE SAME
AND/OR THAT PAPERS SUBMITTED INCLUDES NO NEW MATTER**

4. I hereby state:

(complete applicable item A and/or B)

- A. ☒ Each computer readable form submitted in this application, including those forms requested to be transferred from applicant's other application, is the same as the "Sequence Listing" to which it is indicated to relate.
- B. ☒ All papers accompanying this submission, or for which a request for transfer from applicants' other application, introduce no new matter.

STATUS

5. Applicant is

- ☒ a small entity. A statement:
- ☒ is attached.
- ☐ was already filed.
- ☐ other than a small entity.

(Submission—Nucleotide and/or Amino Acid Sequence [9-37]—page 3 of 6)

EXTENSION OF TERM

6.

NOTE: "Extension of Time in Patent Cases (Supplement Amendments)—If a timely and complete response has been filed after a Non-Final Office Action, an extension of time is not required to permit filing and/or entry of an additional amendment after expiration of the shortened statutory period.

If a timely response has been filed after a Final Office Action, an extension of time is required to permit filing and/or entry of a Notice of Appeal or filing and/or entry of an additional amendment after expiration of the shortened statutory period unless the timely-filed response placed the application in condition for allowance. Of course, if a Notice of Appeal has been filed within the shortened statutory period, the period has ceased to run." Notice of Dec. 10, 1985 (1061 O.G. 34-35).

NOTE: See 37 C.F.R. § 1.645 for extensions of time in interference proceedings and 37 C.F.R. § 1.550(c) for extensions of time in reexamination proceedings.

7. The proceedings herein are for a patent application and the provisions of 37 C.F.R. § 1.136 apply.

(complete (a) or (b) as applicable)

- (a) ☐ Applicant petitions for an extension of time under 37 C.F.R. § 1.136 (fees: 37 C.F.R. § 1.17(a)(1)-(4)) for the total number of months checked below:

Extension (months)	Fee for other than small entity	Fee for small entity
<input type="checkbox"/> one month	\$ 110.00	\$ 55.00
<input type="checkbox"/> two months	\$ 380.00	\$ 190.00
<input type="checkbox"/> three months	\$ 870.00	\$ 435.00
<input type="checkbox"/> four months	\$ 1,360.00	\$ 680.00

Fee: \$ _____

If an additional extension of time is required, please consider this a petition therefor.

(check and complete the next item, if applicable)

- ☐ An extension for _____ months has already been secured. The fee paid therefor of \$_____ is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request \$ _____

OR

- (b) ☒ Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition for extension of time.

FEE PAYMENT

8. ☐ Attached is a check in the sum of \$ _____
☐ Charge Account No. _____ the sum of \$ _____
A duplicate of this transmittal is attached.

(Submission—Nucleotide and/or Amino Acid Sequence [9-37]—page 4 of 6)

FEE DEFICIENCY

9.

NOTE: If there is a fee deficiency and there is no authorization to charge an account, additional fees are necessary to cover the additional time consumed in making up the original deficiency. If the maximum, six-month period has expired before the deficiency is noted and corrected, the application is held abandoned. In those instances where authorization to charge is included, processing delays are encountered in returning the papers to the PTO Finance Branch in order to apply these charges prior to action on the cases. Authorization to charge the deposit account for any fee deficiency should be checked. See the Notice of April 7, 1986, 1065 O.G. 31-33.

10. ☒ If any additional extension and/or fee is required, charge

Account No. 13-0610

SIGNATURE(s)

Ian C. McLeod

(type or print name of person signing statement)



Signature

10/5/99

Date

2190 Commons Parkway

P.O. Address of Signatory

Okemos, Michigan 48864

(if applicable)

Telephone No. (517) 347-4100

Reg. No. 20,931

Customer No.: 21036

- ☐ Inventor(s)
☐ Assignee of complete interest
☐ Person authorized to sign on behalf of assignee
☒ Practitioner of record
☐ Filed under Rule 34(a)
☐ Registration No. _____
☐ Other _____

(specify identity of declarant)

(complete the following, if applicable)

(type name of assignee)

Address of assignee

Title of person authorized to sign on behalf of assignee

A "STATEMENT UNDER 37 C.F.R. § 3.73(b)" is attached.

Assignment recorded in PTO on _____

Reel _____ Frame _____

Reg. No.:

SIGNATURE OF PRACTITIONER

(type or print name of practitioner)

Tel. No.: ()

P.O. Address

Customer No.:

SEQUENCE LISTING

<110> Dilley, David R
Kadyrzhanova, Dina K
Wang, Zhenyong
Warner, Toni M

<120> Modified Synthetases To Produce Penicillins and
Cephalosporins Under the Control of Bicarbonate

<130> MSU 41-453

<140>

<141>

<160> 18

<170> PatentIn Ver. 2.0

<210> 1

<211> 331

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Emericella nidulans strain b1A1

<220>

<221> MUTAGEN

<222> (212)

<223> Glu212 in native IPNS modified to Arg

<400> 1

Met	Gly	Ser	Val	Ser	Lys	Ala	Asn	Val	Pro	Lys	Ile	Asp	Val	Ser	Pro
1					5					10					15

Leu	Phe	Gly	Asp	Asp	Gln	Ala	Ala	Lys	Met	Arg	Val	Ala	Gln	Ile	
			20					25					30		

Asp	Ala	Ala	Ser	Arg	Asp	Thr	Gly	Phe	Phe	Tyr	Ala	Val	Asn	His	Gly
			35				40					45			

Ile	Asn	Val	Gln	Arg	Leu	Ser	Gln	Lys	Thr	Lys	Glu	Phe	His	Met	Ser
		50				55					60				

Ile	Thr	Pro	Glu	Glu	Lys	Trp	Asp	Leu	Ala	Ile	Arg	Ala	Tyr	Asn	Lys
						70				75					80

Glu His Gln Asp Gln Val Arg Ala Gly Tyr Tyr Leu Ser Ile Pro Gly
85 90 95

Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asn Phe Thr Pro
100 105 110

Asp His Pro Arg Ile Gln Ala Lys Thr Pro Thr His Glu Val Asn Val
115 120 125

Trp Pro Asp Glu Thr Lys His Pro Gly Phe Gln Asp Phe Ala Glu Gln
130 135 140

Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Leu Leu Lys Gly Tyr
145 150 155 160

Ala Leu Ala Leu Gly Lys Glu Glu Asn Phe Phe Ala Arg His Phe Lys
165 170 175

Pro Asp Asp Thr Leu Ala Ser Val Val Leu Ile Arg Tyr Pro Tyr Leu
180 185 190

Asp Pro Tyr Pro Glu Ala Ala Ile Lys Thr Ala Ala Asp Gly Thr Lys
195 200 205

Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val Leu Tyr
210 215 220

Gln Ser Asn Val Gln Asn Leu Gln Val Glu Thr Ala Ala Gly Tyr Gln
225 230 235 240

Asp Ile Glu Ala Asp Asp Thr Gly Tyr Leu Ile Asn Cys Gly Ser Tyr
245 250 255

Met Ala His Leu Thr Asn Asn Tyr Tyr Lys Ala Pro Ile His Arg Val
260 265 270

Lys Trp Val Asn Ala Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu
275 280 285

Gly Tyr Asp Ser Val Ile Asp Pro Phe Asp Pro Arg Glu Pro Asn Gly
290 295 300

Lys Ser Asp Arg Glu Pro Leu Ser Tyr Gly Asp Tyr Leu Gln Asn Gly
305 310 315 320

Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr
325 330

<210> 2
 <211> 331
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: modified IPNS
 from Emericella nidulans strain FGSC-4

<220>
 <221> MUTAGEN
 <222> (212)
 <223> Glu212 in native IPNS modified to Arg

<400> 2
 Met Gly Ser Val Ser Lys Ala Asn Val Pro Lys Ile Asp Val Ser Pro
 1 5 10 15
 Leu Phe Gly Asp Asp Gln Ala Ala Lys Met Arg Val Ala Gln Gln Ile
 20 25 30
 Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn His Gly
 35 40 45
 Ile Asn Val Gln Arg Leu Ser Gln Lys Thr Lys Glu Phe His Met Ser
 50 55 60
 Ile Thr Pro Glu Glu Lys Trp Asp Leu Ala Ile Arg Ala Tyr Asn Lys
 65 70 75 80
 Glu His Gln Asp Gln Val Arg Ala Gly Tyr Tyr Leu Ser Ile Pro Gly
 85 90 95
 Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asn Phe Thr Pro
 100 105 110
 Asp His Pro Arg Ile Gln Ala Lys Thr Pro Thr His Glu Val Asn Val
 115 120 125
 Trp Pro Asp Glu Thr Lys His Pro Gly Phe Gln Asp Phe Ala Glu Gln
 130 135 140
 Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Leu Leu Lys Gly Tyr
 145 150 155 160
 Ala Leu Ala Leu Gly Lys Glu Glu Asn Phe Phe Ala Arg His Phe Lys

165	170	175
Pro Asp Asp Thr Leu Ala Ser Val Val Leu Ile Arg Tyr Pro Tyr Leu		
180	185	190
Asp Pro Tyr Pro Glu Ala Ala Ile Lys Thr Ala Ala Asp Gly Thr Lys		
195	200	205
Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val Leu Tyr		
210	215	220
Gln Ser Asn Val Gln Asn Leu Gln Val Glu Thr Ala Ala Gly Tyr Gln		
225	230	235
Asp Ile Glu Ala Asp Asp Thr Gly Tyr Leu Ile Asn Cys Gly Ser Tyr		
245	250	255
Met Ala His Leu Thr Asn Asn Tyr Tyr Lys Ala Pro Ile His Arg Val		
260	265	270
Lys Trp Val Asn Ala Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu		
275	280	285
Gly Tyr Asp Ser Val Ile Asp Pro Phe Asp Pro Arg Glu Pro Asn Gly		
290	295	300
Lys Ser Asp Arg Glu Pro Leu Ser Tyr Gly Asp Tyr Leu Gln Asn Gly		
305	310	315
Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr		
325	330	

<210> 3

<211> 331

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Emericella nidulans strain bioA1

<220>

<221> MUTAGEN

<222> (212)

<223> Glu212 in native IPNS modified to Arg

<400> 3

Met Gly Ser Val Ser Lys Ala Asn Val Pro Lys Ile Asp Val Ser Pro
1 5 10 15

Leu Phe Gly Asp Asp Gln Ala Ala Lys Met Arg Val Ala Gln Gln Ile
20 25 30

Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn His Gly
35 40 45

Ile Asn Val Gln Arg Leu Ser Gln Lys Thr Lys Glu Phe His Met Ser
50 55 60

Ile Thr Pro Glu Glu Lys Trp Asp Leu Ala Ile Arg Ala Tyr Asn Lys
65 70 75 80

Glu His Gln Asp Gln Val Arg Ala Gly Tyr Tyr Leu Ser Ile Pro Gly
85 90 95

Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asn Phe Thr Pro
100 105 110

Asp His Pro Arg Ile Gln Ala Lys Thr Pro Thr His Glu Val Asn Val
115 120 125

Tyr Pro Asp Glu Thr Lys His Pro Gly Phe Gln Asp Phe Ala Glu Gln
130 135 140

Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Leu Leu Lys Gly Tyr
145 150 155 160

Ala Leu Ala Leu Gly Lys Glu Glu Asn Phe Phe Ala Arg His Phe Lys
165 170 175

Pro Asp Asp Thr Leu Ala Ser Val Val Leu Ile Arg Tyr Pro Tyr Leu
180 185 190

Asp Pro Tyr Pro Glu Ala Ala Ile Lys Thr Ala Ala Asp Gly Thr Lys
195 200 205

Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val Leu Tyr
210 215 220

Gln Ser Asn Val Gln Asn Leu Gln Val Glu Thr Ala Ala Gly Tyr Gln
225 230 235 240

Asp Ile Glu Ala Asp Asp Thr Gly Tyr Leu Ile Asn Cys Gly Ser Tyr
245 250 255

Met Ala His Leu Thr Asn Asn Tyr Tyr Lys Ala Pro Ile His Arg Val
260 265 270

Lys Trp Val Asn Ala Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu
275 280 285

Gly Tyr Asp Ser Val Ile Asp Pro Phe Asp Pro Arg Glu Pro Asn Gly
290 295 300

Lys Ser Asp Arg Glu Pro Leu Ser Tyr Gly Asp Tyr Leu Gln Asn Gly
305 310 315 320

Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr
325 330

<210> 4

<211> 331

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Penicillium chrysogenum

<220>

<221> MUTAGEN

<222> (212)

<223> Glu212 in native IPNS modified to Arg

<400> 4

Met Ala Ser Thr Pro Lys Ala Asn Val Pro Lys Ile Asp Val Ser Pro
1 5 10 15

Leu Phe Gly Asp Asn Met Glu Glu Lys Met Lys Val Ala Arg Ala Ile
20 25 30

Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn His Gly
35 40 45

Val Asp Val Lys Arg Leu Ser Asn Lys Thr Arg Glu Phe His Phe Ser
50 55 60

Ile Thr Asp Glu Glu Lys Trp Asp Leu Ala Ile Arg Ala Tyr Asn Lys
65 70 75 80

Glu His Gln Asp Gln Ile Arg Ala Gly Tyr Tyr Leu Ser Ile Pro Glu
85 90 95

Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asn Phe Lys Pro
100 105 110

Asp His Pro Leu Ile Gln Ser Lys Thr Pro Thr His Glu Val Asn Val
115 120 125

Trp Pro Asp Glu Lys Lys His Pro Gly Phe Arg Glu Phe Ala Glu Gln
130 135 140

Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Leu Leu Arg Gly Tyr
145 150 155 160

Ala Leu Ala Leu Gly Lys Glu Glu Asp Phe Phe Ser Arg His Phe Lys
165 170 175

Lys Glu Asp Ala Leu Ser Ser Val Val Leu Ile Arg Tyr Pro Tyr Leu
180 185 190

Asn Pro Ile Pro Pro Ala Ala Ile Lys Thr Ala Glu Asp Gly Thr Lys
195 200 205

Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val Leu Tyr
210 215 220

Gln Ser Asp Val Ala Asn Leu Gln Val Glu Met Pro Gln Gly Tyr Leu
225 230 235 240

Asp Ile Glu Ala Asp Asp Asn Ala Tyr Leu Val Asn Cys Gly Ser Tyr
245 250 255

Met Ala His Ile Thr Asn Asn Tyr Tyr Pro Ala Pro Ile His Arg Val
260 265 270

Lys Trp Val Asn Glu Glu Arg Gln Ser Leu Pro Phe Phe Val Asn Leu
275 280 285

Gly Phe Asn Asp Thr Val Gln Pro Trp Asp Pro Ser Lys Glu Asp Gly
290 295 300

Lys Thr Asp Gln Arg Pro Ile Ser Tyr Gly Asp Tyr Leu Gln Asn Gly
305 310 315 320

Leu Val Ser Leu Ile Asn Lys Asn Gly Gln Thr
325 330

<210> 5

<211> 329
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: modified IPNS
 from Streptomyces clavuligerus

<220>
 <221> MUTAGEN
 <222> (210)
 <223> Glu210 in native IPNS modified to Arg

<400> 5
 Met Pro Val Leu Met Pro Ser Ala His Val Pro Thr Ile Asp Ile Ser
 1 5 10 15

Pro Leu Phe Gly Thr Asp Ala Ala Ala Lys Lys Arg Val Ala Glu Glu
 20 25 30

Ile His Gly Ala Cys Arg Gly Ser Gly Phe Phe Tyr Ala Thr Asn His
 35 40 45

Gly Val Asp Val Gln Gln Leu Gln Asp Val Val Asn Glu Phe His Gly
 50 55 60

Ala Met Thr Asp Gln Glu Lys His Asp Leu Ala Ile His Ala Tyr Asn
 65 70 75 80

Pro Asp Asn Pro His Val Arg Asn Gly Tyr Tyr Lys Ala Val Pro Gly
 85 90 95

Arg Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asp Phe Gly Glu
 100 105 110

Asp His Pro Met Ile Ala Ala Gly Thr Pro Met His Glu Val Asn Leu
 115 120 125

Trp Pro Asp Glu Glu Arg His Pro Arg Phe Arg Pro Phe Cys Glu Gly
 130 135 140

Tyr Tyr Arg Gln Met Leu Lys Leu Ser Thr Val Leu Met Arg Gly Leu
 145 150 155 160

Ala Leu Ala Leu Gly Arg Pro Glu His Phe Asp Ala Ala Leu Ala
 165 170 175

Glu Gln Asp Ser Leu Ser Ser Val Ser Leu Ile Arg Tyr Pro Tyr Leu

180	185	190
Glu Glu Tyr Pro Pro Val Lys Thr Gly Pro Asp Gly Gln Leu Leu Ser		
195	200	205
Phe Arg Asp His Leu Asp Val Ser Met Ile Thr Val Leu Phe Gln Thr		
210	215	220
Gln Val Gln Asn Leu Gln Val Glu Thr Val Asp Gly Trp Arg Asp Ile		
225	230	235
Pro Thr Ser Glu Asn Asp Phe Leu Val Asn Cys Gly Thr Tyr Met Ala		
245	250	255
His Val Thr Asn Asp Tyr Phe Pro Ala Pro Asn His Arg Val Lys Phe		
260	265	270
Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu Asn Gly Gly His		
275	280	285
Glu Ala Val Ile Glu Pro Phe Val Pro Glu Gly Ala Ser Glu Glu Val		
290	295	300
Arg Asn Glu Ala Leu Ser Tyr Gly Asp Tyr Leu Gln His Gly Leu Arg		
305	310	315
		320
Ala Leu Ile Val Lys Asn Gly Gln Thr		
325		

<210> 6

<211> 338

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Acremonium chrysogenum

<220>

<221> MUTAGEN

<222> (214)

<223> Glu214 in native IPNS modified to Arg

<400> 6

Met Gly Ser Val Pro Val Pro Val Ala Asn Val Pro Arg Ile Asp Val
1 5 10 15

Ser Pro Leu Phe Gly Asp Asp Lys Glu Lys Lys Leu Glu Val Ala Arg
20 25 30

Ala Ile Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn
35 40 45

His Gly Val Asp Leu Pro Trp Leu Ser Arg Glu Thr Asn Lys Phe His
50 55 60

Met Ser Ile Thr Asp Glu Glu Lys Trp Gln Leu Ala Ile Arg Ala Tyr
65 70 75 80

Asn Lys Glu His Glu Ser Gln Ile Arg Ala Gly Tyr Tyr Leu Pro Ile
85 90 95

Pro Gly Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Ser Phe
100 105 110

Ser Pro Asp His Pro Arg Ile Lys Glu Pro Thr Pro Met His Glu Val
115 120 125

Asn Val Trp Pro Asp Glu Ala Lys His Pro Gly Phe Arg Ala Phe Ala
130 135 140

Glu Lys Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Val Leu Arg
145 150 155 160

Gly Tyr Ala Leu Ala Leu Gly Arg Asp Glu Asp Phe Phe Thr Arg His
165 170 175

Ser Arg Arg Asp Thr Thr Leu Ser Ser Val Val Leu Ile Arg Tyr Pro
180 185 190

Tyr Leu Asp Pro Tyr Pro Glu Pro Ala Ile Lys Thr Ala Asp Asp Gly
195 200 205

Thr Lys Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val
210 215 220

Leu Tyr Gln Ser Asp Val Gln Asn Leu Gln Val Lys Thr Pro Gln Gly
225 230 235 240

Trp Gln Asp Ile Gln Ala Asp Asp Thr Gly Phe Leu Ile Asn Cys Gly
245 250 255

Ser Tyr Met Ala His Ile Thr Asp Asp Tyr Tyr Pro Ala Pro Ile His
260 265 270

Arg Val Lys Trp Val Asn Glu Glu Arg Gln Ser Leu Pro Phe Phe Val
275 280 285

Asn Leu Gly Trp Glu Asp Thr Ile Gln Pro Trp Asp Pro Ala Thr Ala
290 295 300

Lys Asp Gly Ala Lys Asp Ala Ala Lys Asp Lys Pro Ala Ile Ser Tyr
305 310 315 320

Gly Glu Tyr Leu Gln Gly Gly Leu Arg Gly Leu Ile Asn Lys Asn Gly
325 330 335

Gln Thr

<210> 7

<211> 338

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from Acremonium chrysogenum strain M8650

<220>

<221> MUTAGEN

<222> (214)

<223> Glu214 in native IPNS modified to Arg

<400> 7

Met Gly Ser Val Pro Val Pro Val Ala Asn Val Pro Arg Ile Asp Val
1 5 10 15

Ser Pro Leu Phe Gly Asp Asp Lys Glu Lys Lys Leu Glu Val Ala Arg
20 25 30

Ala Ile Asp Ala Ala Ser Arg Asp Thr Gly Phe Phe Tyr Ala Val Asn
35 40 45

His Gly Val Asp Leu Pro Trp Leu Ser Arg Glu Thr Asn Lys Phe His
50 55 60

Met Ser Ile Thr Asp Glu Glu Lys Trp Gln Leu Ala Ile Arg Ala Tyr
65 70 75 80

Asn Lys Glu His Glu Ser Gln Ile Arg Ala Gly Tyr Tyr Leu Pro Ile
85 90 95

Pro Gly Lys Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Ser Phe
100 105 110

Ser Pro Asp His Pro Arg Ile Lys Glu Pro Thr Pro Met His Glu Val
115 120 125

Asn Val Trp Pro Asp Glu Ala Lys His Pro Gly Phe Arg Ala Phe Ala
130 135 140

Glu Lys Tyr Tyr Trp Asp Val Phe Gly Leu Ser Ser Ala Val Leu Arg
145 150 155 160

Gly Tyr Ala Leu Ala Leu Gly Arg Asp Glu Asp Phe Phe Thr Arg His
165 170 175

Phe Arg Arg Asp Thr Thr Leu Ser Ser Val Val Leu Ile Arg Tyr Pro
180 185 190

Tyr Leu Asp Pro Tyr Pro Glu Pro Ala Ile Lys Thr Ala Asp Asp Gly
195 200 205

Thr Lys Leu Ser Phe Arg Trp His Glu Asp Val Ser Leu Ile Thr Val
210 215 220

Leu Tyr Gln Ser Asp Val Gln Asn Leu Gln Val Lys Thr Pro Gln Gly
225 230 235 240

Trp Gln Asp Ile Gln Ala Asp Asp Thr Gly Phe Leu Ile Asn Cys Gly
245 250 255

Ser Tyr Met Ala His Ile Thr Asp Asp Tyr Tyr Pro Ala Pro Ile His
260 265 270

Arg Val Lys Trp Val Asn Glu Glu Arg Gln Ser Leu Pro Phe Phe Val
275 280 285

Asn Leu Gly Trp Glu Asp Thr Ile Gln Pro Trp Asp Pro Ala Thr Ala
290 295 300

Lys Asp Gly Ala Lys Asp Ala Ala Lys Asp Lys Pro Ala Ile Ser Tyr
305 310 315 320

Gly Glu Tyr Leu Gln Gly Gly Leu Arg Gly Leu Ile Asn Lys Asn Gly
325 330 335

Gln Thr

<210> 8
 <211> 321
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Description of Artificial Sequence: modified IPNS
 from Streptomyces cattleya

<220>
 <221> MUTAGEN
 <222> (211)
 <223> Glu211 in native IPNS modified to Arg

<400> 8
 Met Pro Val Leu Met Pro Ser Ala Asp Val Pro Thr Ile Asp Ile Ser
 1 5 10 15
 Pro Gln Leu Phe Gly Thr Asp Pro Thr Pro Arg Arg Thr Ser Arg Gly
 20 25 30
 Arg Ser Thr Arg Pro Ala Arg Gly Ser Gly Phe Phe Tyr Ala Ser His
 35 40 45
 His Gly Ile Asp Val Arg Arg Leu Gln Thr Trp Ser Asn Glu Ser Thr
 50 55 60
 Thr Met Thr Asp Gln Arg Ser Thr Thr Trp Arg Ser Thr Arg Tyr Asn
 65 70 75 80
 Glu Asn Asn Ser His Val Arg Asn Gly Tyr Tyr Met Ala Arg Pro Gly
 85 90 95
 Arg Glu Thr Val Glu Ser Trp Cys Tyr Leu Asn Pro Ser Phe Gly Glu
 100 105 110
 Asp His Pro Met Met Lys Ala Gly Thr Pro Met His Glu Val Asn Val
 115 120 125
 Trp Pro Asp Glu Glu Arg His Pro Asp Phe Gly Ser Phe Gly Glu Gln
 130 135 140
 Tyr His Arg Glu Val Ser Ala Ser Arg Arg Cys Cys Cys Gly Ala Ser
 145 150 155 160
 Arg Trp Arg Arg Gln Ala Gly Glu Ser Ser Ser Asn Glu Val Thr Glu

165	170	175
Glu Asp Thr Leu Ser Ala Val Ser Met Ile Arg Tyr Pro Tyr Leu Asp 180	185	190
Pro Tyr Pro Glu Ala Ala Ile Lys Thr Gly Pro Asp Gly Thr Arg Leu 195	200	205
Ser Phe Arg Asp His Leu Asp Val Ser Met Ile Thr Val Leu Ser Lys 210	215	220
Thr Glu Val Gln Asn Leu Gln Val Glu Thr Val Asp Gly Trp Gln Ser 225	230	235
Leu Pro Thr Ser Gly Glu Asn Phe Leu Ile Asn Cys Gly Thr Tyr Leu 245	250	255
Gly Tyr Leu Thr Asn Asp Tyr Phe Pro Ala Pro Asn His Arg Val Lys 260	265	270
Tyr Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu His Ala Gly 275	280	285
Gln Asn Ser Val Met Lys Pro Phe Thr Arg Arg Thr Gly Asp Arg Lys 290	295	300
Leu Asn Pro Ala Val Thr Tyr Gly Glu Tyr Leu Gln Glu Gly Phe Thr 305	310	315
		320

Arg

<210> 9

<211> 329

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from *Streptomyces clavuligerus* strain NRRL 3585

<220>

<221> MUTAGEN

<222> (210)

<223> Glu210 in native IPNS modified to Arg

<400> 9

Met Pro Val Leu Met Pro Ser Ala His Val Pro Thr Ile Asp Ile Ser
1 5 10 15

Pro Leu Phe Gly Thr Asp Ala Ala Ala Lys Lys Arg Val Ala Glu Glu
20 25 30

Ile His Gly Ala Cys Arg Gly Ser Gly Phe Phe Tyr Ala Thr Asn His
35 40 45

Gly Val Asp Val Gln Gln Leu Gln Asp Val Val Asn Glu Phe His Gly
50 55 60

Ala Met Thr Asp Gln Glu Lys His Asp Leu Ala Ile His Ala Tyr Asn
65 70 75 80

Pro Asp Asn Pro His Val Arg Asn Gly Tyr Tyr Lys Ala Val Pro Gly
85 90 95

Arg Lys Ala Val Glu Ser Phe Cys Tyr Leu Asn Pro Asp Phe Gly Glu
100 105 110

Asp His Pro Met Ile Ala Ala Gly Thr Pro Met His Glu Val Asn Leu
115 120 125

Trp Pro Asp Glu Glu Arg His Pro Arg Phe Arg Pro Phe Cys Glu Gly
130 135 140

Tyr Tyr Arg Gln Met Leu Lys Leu Ser Thr Val Leu Met Arg Gly Leu
145 150 155 160

Ala Leu Ala Leu Gly Arg Pro Glu His Phe Phe Asp Ala Ala Leu Ala
165 170 175

Glu Gln Asp Ser Leu Ser Ser Val Ser Leu Ile Arg Tyr Pro Tyr Leu
180 185 190

Glu Glu Tyr Pro Pro Val Lys Thr Gly Pro Asp Gly Gln Leu Leu Ser
195 200 205

Phe Arg Asp His Leu Asp Val Ser Met Ile Thr Val Leu Phe Gln Thr
210 215 220

Gln Val Gln Asn Leu Gln Val Glu Thr Val Asp Gly Trp Arg Asp Ile
225 230 235 240

Pro Thr Ser Glu Asn Asp Phe Leu Val Asn Cys Gly Thr Tyr Met Ala
245 250 255

His Val Thr Asn Asp Tyr Phe Pro Ala Pro Asn His Arg Val Lys Phe
260 265 270

Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu Asn Gly Gly His
275 280 285

Glu Ala Val Ile Glu Pro Phe Val Pro Glu Gly Ala Ser Glu Glu Val
290 295 300

Arg Asn Glu Ala Leu Ser Tyr Gly Asp Tyr Leu Gln His Gly Leu Arg
305 310 315 320

Ala Leu Ile Val Lys Asn Gly Gln Thr
325

<210> 10

<211> 333

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified IPNS
from streptomyces anulatus (S. lipmanii)

<220>

<221> MUTAGEN

<222> (214)

<223> Glu214 in native IPNS modified to Arg

<400> 10

Met Pro Val Leu Met Pro Ser Ala Asp Val Pro Thr Ile Asp Ile Ser
1 5 10 15

Pro Leu Phe Gly Thr Asp Pro Asp Ala Lys Ala His Val Ala Arg Gln
20 25 30

Ile Asn Glu Ala Cys Arg Gly Ser Gly Phe Phe Tyr Ala Ser His His
35 40 45

Gly Ile Asp Val Arg Arg Leu Gln Asp Val Val Asn Glu Phe His Arg
50 55 60

Thr Met Thr Asp Gln Glu Lys His Asp Leu Ala Ile His Ala Tyr Asn
65 70 75 80

Glu Asn Asn Ser His Val Arg Asn Gly Tyr Tyr Met Ala Arg Pro Gly
85 90 95

Arg Lys Thr Val Glu Ser Trp Cys Tyr Leu Asn Pro Ser Phe Gly Glu
100 105 110

Asp His Pro Met Ile Lys Ala Gly Thr Pro Met His Glu Val Asn Val
115 120 125

Trp Pro Asp Glu Glu Arg His Pro Asp Phe Arg Ser Phe Gly Glu Gln
130 135 140

Tyr Tyr Arg Glu Val Phe Arg Leu Ser Lys Val Leu Leu Leu Arg Gly
145 150 155 160

Phe Ala Leu Ala Leu Gly Lys Pro Glu Glu Phe Phe Glu Asn Glu Val
165 170 175

Thr Glu Glu Asp Thr Leu Ser Cys Arg Ser Leu Met Ile Arg Tyr Pro
180 185 190

Tyr Leu Asp Pro Tyr Pro Glu Ala Ala Ile Lys Thr Gly Pro Asp Gly
195 200 205

Thr Arg Leu Ser Phe Arg Asp His Leu Asp Val Ser Met Ile Thr Val
210 215 220

Leu Phe Gln Thr Glu Val Gln Asn Leu Gln Val Glu Thr Val Asp Gly
225 230 235 240

Trp Gln Ser Leu Pro Thr Ser Gly Glu Asn Phe Leu Ile Asn Cys Gly
245 250 255

Thr Tyr Leu Gly Tyr Leu Thr Asn Asp Tyr Phe Pro Ala Pro Asn His
260 265 270

Arg Val Lys Tyr Val Asn Ala Glu Arg Leu Ser Leu Pro Phe Phe Leu
275 280 285

His Ala Gly Gln Asn Ser Val Met Lys Pro Phe His Pro Glu Asp Thr
290 295 300

Gly Asp Arg Lys Leu Asn Pro Ala Val Thr Tyr Gly Glu Tyr Leu Gln
305 310 315 320

Glu Gly Phe His Ala Leu Ile Ala Lys Asn Val Gln Thr
325 330

<210> 11

<211> 21
<212> PRT
<213> Emericella nidulans

<220>
<221> PEPTIDE
<222> (1)..(21)
<223> corresponds to amino acids 205 to 225 of native
IPNS

<400> 11
Asp Gly Thr Lys Leu Ser Phe Glu Trp His Glu Asp Val Ser Leu Ile
1 5 10 15

Thr Val Leu Tyr Gln
20

<210> 12
<211> 21
<212> PRT
<213> Penicillium chrysogenum

<220>
<221> PEPTIDE
<222> (1)..(21)
<223> corresponds to amino acids 205 to 225 of native
IPNS

<400> 12
Asp Gly Thr Lys Leu Ser Phe Glu Trp His Glu Asp Val Ser Leu Ile
1 5 10 15

Thr Val Leu Tyr Gln
20

<210> 13
<211> 21
<212> PRT
<213> Acremonium chrysogenum

<220>
<221> PEPTIDE
<222> (1)..(21)
<223> corresponds to amino acids 207 to ss7 of native
IPNS

<400> 13

Asp Gly Thr Lys Leu Ser Phe Glu Trp His Glu Asp Val Ser Leu Ile
1 5 10 15

Thr Val Leu Tyr Gln
20

<210> 14

<211> 21

<212> PRT

<213> Streptomyces clavuligerus

<220>

<221> PEPTIDE

<222> (1)..(21)

<223> corresponds to amino acids 302 to 223 of native
IPNS

<400> 14

Asp Gly Gln Leu Leu Ser Phe Glu Asp His Leu Asp Val Ser Met Ile
1 5 10 15

Thr Val Leu Phe Gln
20

<210> 15

<211> 21

<212> PRT

<213> Streptomyces cattleya

<220>

<221> PEPTIDE

<222> (1)..(21)

<223> corresponds to amino acids 204 to 224 of native
IPNS

<400> 15

Asp Gly Thr Arg Leu Ser Phe Glu Asp His Leu Asp Val Ser Met Ile
1 5 10 15

Thr Val Leu Ser Glu
20

<210> 16

<211> 21

[illegible] $\langle 220 \rangle$

<222> (1) . . (21)

<400> 16

Thr Val Leu Phe Gln
20

<211> 30

<213> Artificial Sequence

 $\langle 220 \rangle$

<223> Description of Artificial Sequence: mutagenic oligonucleotide primer

<400> 17

ctgagttttg agtggcatcg gqatgtaatc 30

<210> 18

<211> 311

<212> PRT

<213> Artificial Sequence

 $\langle 220 \rangle$

<223> Description of Artificial Sequence: modified DAOCS
from Streptomyces clavuligerus

 $\langle 220 \rangle$

<221> MUTAGEN

<222> (181)

<223> Ala181 in native DAOCS modified to Arg

<400> 18

Met Asp Thr Thr Val Pro Thr Phe Ser Leu Ala Glu Leu Gln Gln Gly
1 5 10 15

Leu His Gln Asp Glu Phe Arg Arg Cys Leu Arg Asp Lys Gly Leu Phe

20					25					30						
Tyr	Leu	Thr	Asp	Cys	Gly	Leu	Thr	Asp	Thr	Glu	Leu	Lys	Ser	Ala	Lys	
35					40					45						
Asp	Leu	Val	Ile	Asp	Phe	Phe	Glu	His	Gly	Ser	Glu	Ala	Glu	Lys	Arg	
50					55					60						
Ala	Val	Thr	Ser	Pro	Val	Pro	Thr	Met	Arg	Arg	Gly	Phe	Thr	Gly	Leu	
65					70					75					80	
Glu	Ser	Glu	Ser	Thr	Ala	Gln	Ile	Thr	Asn	Thr	Gly	Ser	Tyr	Ser	Asp	
85					90					95						
Tyr	Ser	Met	Cys	Tyr	Ser	Met	Gly	Thr	Ala	Asp	Asn	Leu	Phe	Pro	Ser	
100					105					110						
Gly	Asp	Phe	Glu	Arg	Ile	Trp	Thr	Gln	Tyr	Phe	Asp	Arg	Gln	Tyr	Thr	
115					120					125						
Ala	Ser	Arg	Ala	Val	Ala	Arg	Glu	Val	Leu	Arg	Ala	Thr	Gly	Thr	Glu	
130					135					140						
Pro	Asp	Gly	Gly	Val	Glu	Ala	Phe	Leu	Asp	Cys	Glu	Pro	Leu	Leu	Arg	
145					150					155					160	
Phe	Arg	Tyr	Phe	Pro	Gln	Val	Pro	Glu	His	Arg	Ser	Ala	Glu	Glu	Gln	
165					170					175						
Pro	Leu	Arg	Met	Arg	Pro	His	Tyr	Asp	Leu	Ser	Met	Val	Thr	Leu	Ile	
180					185					190						
Gln	Gln	Thr	Pro	Cys	Ala	Asn	Gly	Phe	Val	Ser	Leu	Gln	Ala	Glu	Val	
195					200					205						
Gly	Gly	Ala	Phe	Thr	Asp	Leu	Pro	Tyr	Arg	Pro	Asp	Ala	Val	Leu	Val	
210					215					220						
Phe	Cys	Gly	Ala	Ile	Ala	Thr	Leu	Val	Thr	Gly	Gly	Gln	Val	Lys	Ala	
225					230					235					240	
Pro	Arg	His	His	Val	Ala	Ala	Pro	Arg	Arg	Asp	Gln	Ile	Ala	Gly	Ser	
245					250					255						
Ser	Arg	Thr	Ser	Ser	Val	Phe	Phe	Leu	Arg	Pro	Asn	Ala	Asp	Phe	Thr	
260					265					270						
Phe	Ser	Val	Pro	Leu	Ala	Arg	Glu	Cys	Gly	Phe	Asp	Val	Ser	Leu	Asp	

275

280

285

Gly Glu Thr Ala Thr Phe Gln Asp Trp Ile Gly Gly Asn Tyr Val Asn
290 295 300

Ile Arg Arg Thr Ser Lys Ala
305 310